

Case Report

¹⁸F-FDG Avid in Uterine Leiomyoma: A Case Report

Sunanta Chiewvit MD*

* Division of Nuclear Medicine, Department of Radiology, Siriraj Hospital, Mahidol University, Bangkok, Thailand

The author presents a case of ¹⁸F-FDG avid in uterine leiomyoma. A 32-year old female had Hodgkin's lymphoma stage IVb (the primary lesions at bilateral supraclavicular, right paratracheal, subcarina, intraabdominal, bilateral iliac lymph nodes with liver, spleen and bone marrow involvement). She was sent for ¹⁸F-FDG PET/CT scan for detection of active lymphoma after chemotherapy treatment. The positive finding was hypermetabolic well defined round shape-enhanced lesion at posterior fundus. The SUV max (maximum value of Standard uptake value) was 6.3 and 2.0 x 1.9 CM in size. This lesion on CT finding is compatible with uterine leiomyoma. There is no other area of abnormal activity in the other body parts in the scan finding. After the PET/CT study, the patient was in remission of disease with no treatment. The planning is for follow-up CT. The knowledge of normal variation or false positive finding of ¹⁸F-FDG PET scan in order to get the exact diagnosis can dramatically alter the clinical course or plan of treatment.

Keywords: ¹⁸f-FDG, PET/CT, Uterine leiomyoma

J Med Assoc Thai 2012; 95 (2): 288-92

Full text. e-Journal: <http://www.jmat.mat.or.th>

Fluorine-18 fluorodeoxyglucose positron emission tomography-computed tomography (¹⁸F-FDG PET/CT) is the modality of choice for the diagnosis, staging, and restaging of many malignancies. ¹⁸F-FDG generally accumulates in malignant tumors, it can also accumulate in benign lesions, inflammatory conditions, and normal organ such as brain, heart, liver, spleen, bowel, kidney and urinary bladder. It is very important to know the normal variants as well as the false-positive findings in ¹⁸F-FDG PET/CT study. The knowledge of normal organ uptake, normal variation, or false positive finding from PET scan to get the exact diagnosis can dramatically alter the clinical course or plan of treatment. The present report describes an interesting case of intense FDG uptake in the uterine leiomyoma. Uterine leiomyoma is the most common benign pelvic tumor in women. It is often an incidental finding after investigation. Benign leiomyoma in the uterus usually shows no glucose avidity in the ¹⁸F-FDG PET scan. However, earlier reports have described faint or mild ¹⁸F-FDG accumulation in five uterine leiomyomas⁽¹⁾. The study by Ak I⁽²⁾ shows that ¹⁸F-FDG accumulation was detected in all four

patients suspected of having malignant gynecological tumors and diagnosed as uterine leiomyomas based on histopathological examination. The lesion to background ratio of ¹⁸F-FDG PET/CT are 1.78, 2.1, 2.1 and 2.29, respectively. The study by Chura JC⁽³⁾ showed significant ¹⁸F-FDG uptake in the first case, a woman with breast cancer who underwent ¹⁸F-FDG PET scan as part of a workup for metastatic disease. Although the lesion identified was small, she had remarkably high SUV (Standard uptake value) of 16. In the second case, an adenocarcinoma of unknown primary, PET/CT imaging revealed a hypermetabolic lesion (SUV value of 9.34) within the uterus. This was the most significant evaluation finding of a primary site. At surgical exploration, the lesion was a cellular leiomyoma and ultimately no primary carcinoma was identified for this patient. In the third case, a PET/CT scan done for evaluation of non-Hodgkin's lymphoma revealed a uterine lesion with significantly abnormal metabolic activity (SUV of 6.0). Pathology was ultimately consistent with a stromomyoma.

Case Report

A 32-year old female had Hodgkin's lymphoma stage IVb (Primary lesions at bilateral supraclavicular, right paratracheal, subcarina, intraabdominal, bilateral iliac lymph nodes, liver, spleen, and bone marrow involvement). The PET/CT scan was done for detection of active lymphoma after seven cycles of ABVD

Correspondence to:

Chiewvit S, Division of Nuclear Medicine, Department of Radiology, Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

Phone: 0-2419-6220, Fax: 0-2412-7165

E-mail: siscv@mahidol.ac.th

(Adriamycin, Bleomycin, Vinblastine, and Dacarbazine) one year ago. The whole body image from base of skull to upper thigh was performed using a combined PET/CT scanner (GE discovery STE 16 PET/CT scanner). After an overnight fast, the patient's blood glucose was 77 mg/dl. Intravenous injection of 10.66 mCi of 18-fluoro-2-deoxyglucose (F18 FDG) and a standard uptake period of approximate 60 minutes before contrast enhance CT and PET scan was performed in the same level. The only positive finding was a hypermetabolic well defined round shape enhancing lesion at posterior fundus, with a SUV max 6.3 and 2.0 x 1.9 CM in size (Fig. 1, 2). This lesion on CT finding is compatible with uterine leiomyoma. Neither hypermetabolic nor enlarged lymph node in neck, mediastinum, abdominal, the rest of pelvic was found and no evidence of abnormal activity accumulation in the organ suggested active lymphoma. After the PET/CT study, the patient had consistent remission of disease and had no treatment. Follow-up CT is planned.

Discussion

This interesting case shows a high FDG avid in uterine leiomyoma. The exact mechanism responsible for ^{18}F -FDG accumulation in uterine leiomyoma is unclear. On immunohistochemical analysis of resection of the benign uterine leiomyoma, it has been shown that glucose transporter-1 is positive in endocrine tissue and negative in leiomyoma⁽⁴⁾. Thus, the mechanism of ^{18}F -FDG accumulation is not glucose transporter-1 dependent, unlike in malignancies. Although some various mechanisms have been proposed for this accumulation, uterine leiomyoma has a higher level of basic fibroblast growth factor (bFGF) messenger RNA and increased amounts of bFGF in the extracellular matrix⁽⁵⁾. Basic fibroblast growth factor is an angiogenic growth factor, thus promoting formation of new blood vessels. It also causes proliferation of smooth muscle cells, including leiomyoma and myometrial cells. Moderately intense ^{18}F -FDG accumulation of the leiomyomatous uterus may be explained by the existence of higher levels of these growth factors and receptors⁽²⁾. ^{18}F -FDG uptake in the myomatous process may be related in proliferation of smooth muscle cells due to the metabolic needs. There is also evidence that transforming growth factor beta (TGF β) and granulocyte-macrophage colony-stimulating factor (GM-CSF) may be involved in the pathophysiology of uterine leiomyoma as in other fibrotic processes. Uterine leiomyoma has higher amount of

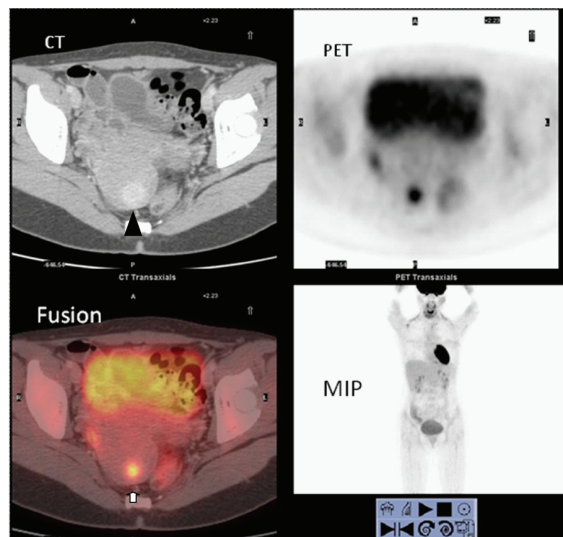


Fig. 1 The axial image of ^{18}F -FDG PET/CT show high ^{18}F FDG uptake (SUV max 6.3) in the well define round shape enhancing lesion at posterior fundus (2.0 x 1.9 CM in size)

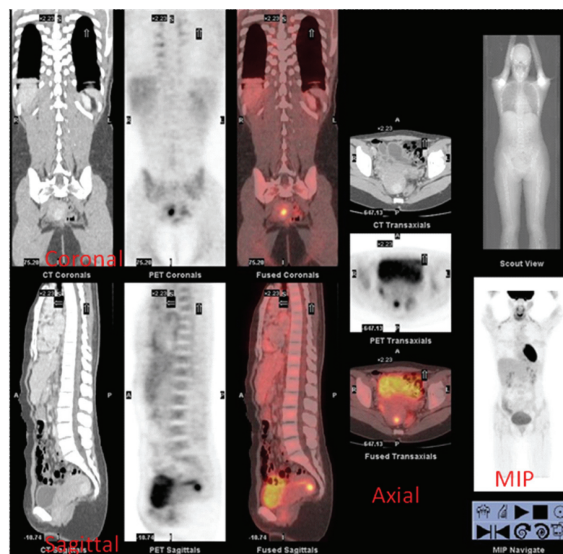


Fig. 2 The coronal, sagittal and axial images of ^{18}F -FDG PET/CT show high ^{18}F FDG uptake (SUV max 6.3) in the well define round shape enhancing lesion at posterior fundus (2.0 x 1.9 CM in size). The MIP (Maximum intensity projection) reveals physiologic activity in the heart, liver, bowel, kidney and urinary bladder

TGF β and TGF β receptor messenger RNA and protein than normal myometrium hypotheses have been proposed⁽²⁾. The most widely accepted theory is the

presence higher level of bFGF, TGF β and GM-CSF and receptors. Another hypothesis is the increased vascularity of leiomyoma. Chura et al⁽³⁾ demonstrated that vascularity, but not the Ki-67 (proliferative) index differs between PET positive uterine leiomyoma and PET negative uterine leiomyoma. One hypothesis to account for the positive PET scans reported above relates to the size of the leiomyoma. The large uterine leiomyoma lesion is associated with neoplasm. The increased size could translate into increased metabolic demands, which then results in an increased ¹⁸F-FDG uptake. Kao was the first to describe ¹⁸F-FDG uptake in a huge uterine myoma⁽⁶⁾. In this case report, a 10.5 x 12 cm leiomyoma was detected on ¹⁸F-FDG PET imaging. In the paper from Chura et al⁽³⁾, the uterine leiomyoma are small in comparison 1.3 cm, 3.8 cm and 4.9 cm in the largest dimension. The study by Kitajima K⁽⁷⁾ revealed the mean value of long diameter of uterine leiomyomas was 48.8 \pm 28.5 mm (range 20 to 133mm). There was a mild positive correlation between maximum SUV and size (r = 0.35, p = 0.011). There was no significant correlation between average SUV and size (r = -0.0092, p = 0.52). Considering age, there was a moderate negative correlation between maximum SUV and age (r = -0.43, p = 0.00016) as well as a mild negative correlation between average SUV and age (r = -0.31, p = 0.029). The mean values of the maximum and average SUVs for the 61 uterine leiomyoma were 2.34 \pm 0.75 (range 1.59 to 5.15) and 1.74 \pm 0.50 (range 0.66 to 3.95), respectively. Ten of 61 uterine leiomyomas showed the value of maximum SUV higher than 2.5 (17%). Uterine leiomyomas with FDG uptake are more common in premenopausal women than postmenopausal women⁽⁸⁾ with uterine leiomyomas. Seventeen patients of 164 (10.4%) was higher than that in post-menopausal women with uterine leiomyomas in four patient of 338 women (1.2%). The incidence was statistically significantly higher in premenopausal women than in post-menopausal women (Chi-square, p < 0.001). The SUV max of premenopausal women with uterine leiomyomas is 5.3 \pm 2.9 (range 3.5-16.0).

The SUV max of postmenopausal women with uterine leiomyomas is 6.1 \pm 2.3 (range 3.7-8.0). Abundant cellularity and hormonal dependency may explain a part of mechanism of FDG uptake in uterine leiomyomas. It is important to know change and newly appearing FDG uptake does not necessary mean malignant transformation. The differential between uterine leiomyosarcoma and uterine leiomyoma by SUV of α -(¹⁸F) fluoro-17 β -estradiol and ¹⁸F-fluorodeoxyglucose was studied by Tsujikawa T⁽⁹⁾ for thirty-eight pre-treatment patients with uterine tumors that were suspected of being malignant at cytological analysis. The result is presented in Table 1.

¹⁸F-FDG uptake in patients with endometrial carcinoma was significantly higher than it was in those with hyperplasia, whereas ¹⁸F-FES (18F-fluoro-17-estradiol) uptake was significantly lower in patients with endometrial carcinoma than it was in patients with endometrial hyperplasia. The uterine leiomyosarcoma showed a higher concentration for ¹⁸F-FDG and a lower accumulation for ¹⁸F-FES contrast with uterine leiomyoma is low concentration for ¹⁸F-FDG and higher accumulation for ¹⁸F-FES. There are some pitfalls of ¹⁸F-FDG-PET in gynecologic category. There are physiologic ¹⁸F-FDG endometrial and ovarian uptakes in premenopausal women. Kim et al⁽¹⁰⁾ reported that some physiologic 18F-FDG accumulation of ovary around the time of ovulation and during the early luteal phase of the menstrual cycle. Lerman et al⁽¹¹⁾ reported the increased endometrial ¹⁸F-FDG uptake in menstrual and ovulation phase. Uterine leiomyoma by itself is not an indication for the treatment except severe pains, fast growth rate of the nodule, arising suspicious about the malignancy uterine leiomyoma should not be indicated for surgical treatment. The management of uterine leiomyoma with increased ¹⁸F-FDG uptake will be closely followed-up and the only case with fast growth of the uterine tumors will be operated on due to the possibility of malignancy. In Tsukada H study with three positive results of ¹⁸F-FDG, there was no case of fast growth of the

Table 1. The mean of SUV both α -(¹⁸F) fluoro-17 β -estradiol and ¹⁸F-fluorodeoxyglucose each uterine tumor are given in the Table

Tumor	No. of patients	FES	FDG	Statistical significant
Endometrial carcinoma	9	3.8 \pm 1.8 (1.3-6.9)	9.6 \pm 3.3 (3.7-15.2)	p < 0.005
Endometrial hyperplasia	4	7.0 \pm 2.9 (4.5-11.0)	1.7 \pm 0.3 (1.3-1.9)	p < 0.05
Leiomyosarcoma	4	1.6 \pm 0.6 (0.9-2.3)	6.4 \pm 4.3 (2.4-10.2)	Not significant
Leiomyoma	21	4.2 \pm 2.4 (1.6-10.5)	2.2 \pm 1.1 (1.3-5.6)	p < 0.005

myomatous uterus⁽¹²⁾. In Yoshida Y study⁽¹³⁾ no differences were seen in uterine benign tumor ¹⁸F-FDG uptake among the various menstrual phases. There was a slightly lower SUV in the proliferative phase than in the other phase. It follows from that the high positive ¹⁸F-FDG uptake as a preoperative finding in postmenopausal women may be enough indication for surgical treatment and a negative ¹⁸F-FDG PET finding indicates clearly a benign lesion in both premenopausal and postmenopausal women. Furthermore, in the present retrospective study, as for timing of ¹⁸F-FDG PET examination during various menstrual cycles in premenopausal women. The PET examination during the proliferative phase would be better for assessment of the reduction uterine leiomyoma false positive cases.

Conclusion

Possibility of ¹⁸F-FDG accumulation in the lower pelvis caused by benign uterine leiomyoma must be kept in mind and CT scan during PET scan can help in accurate interpretation ¹⁸F-FDG accumulation in uterine leiomyoma.

Potential conflicts of interest

None.

References

- Zor E, Stokkel MP, Ozalp S, Vardareli E, Yalcin OT, Ak I. F18-FDG coincidence-PET in patients with suspected gynecological malignancy. *Acta Radiol* 2006; 47: 612-7.
- Ak I, Ozalp S, Yalcin OT, Zor E, Vardareli E. Uptake of 2-[18F]fluoro-2-deoxy-D-glucose in uterine leiomyoma: imaging of four patients by coincidence positron emission tomography. *Nucl Med Commun* 2004; 25: 941-5.
- Chura JC, Truskinovsky AM, Judson PL, Johnson L, Geller MA, Downs LS, Jr. Positron emission tomography and leiomyomas: clinicopathologic analysis of 3 cases of PET scan-positive leiomyomas and literature review. *Gynecol Oncol* 2007; 104: 247-52.
- Shida M, Murakami M, Tsukada H, Ishiguro Y, Kikuchi K, Yamashita E, et al. F-18 fluorodeoxyglucose uptake in leiomyomatous uterus. *Int J Gynecol Cancer* 2007; 17: 285-90.
- Mangrulkar RS, Ono M, Ishikawa M, Takashima S, Klagsbrun M, Nowak RA. Isolation and characterization of heparin-binding growth factors in human leiomyomas and normal myometrium. *Biol Reprod* 1995; 53: 636-46.
- Kao CH. FDG uptake in a huge uterine myoma. *Clin Nucl Med* 2003; 28: 249.
- Kitajima K, Murakami K, Yamasaki E, Kaji Y, Sugimura K. Standardized uptake values of uterine leiomyoma with 18F-FDG PET/CT: variation with age, size, degeneration, and contrast enhancement on MRI. *Ann Nucl Med* 2008; 22: 505-12.
- Nishizawa S, Inubushi M, Kido A, Miyagawa M, Inoue T, Shinohara K, et al. Incidence and characteristics of uterine leiomyomas with FDG uptake. *Ann Nucl Med* 2008; 22: 803-10.
- Tsujikawa T, Yoshida Y, Mori T, Kurokawa T, Fujibayashi Y, Kotsuji F, et al. Uterine tumors: pathophysiologic imaging with 16alpha-[18F] fluoro-17beta-estradiol and 18F fluorodeoxyglucose PET—initial experience. *Radiology* 2008; 248: 599-605.
- Kim SK, Kang KW, Roh JW, Sim JS, Lee ES, Park SY. Incidental ovarian 18F-FDG accumulation on PET: correlation with the menstrual cycle. *Eur J Nucl Med Mol Imaging* 2005; 32: 757-63.
- Lerman H, Metser U, Grisaru D, Fishman A, Lievshitz G, Even-Sapir E. Normal and abnormal 18F-FDG endometrial and ovarian uptake in pre- and postmenopausal patients: assessment by PET/CT. *J Nucl Med* 2004; 45: 266-71.
- Tsukada H, Murakami M, Shida M, Kikuchi K, Watanabe M, Yasuda S, et al. 18F-fluorodeoxyglucose uptake in uterine leiomyomas in healthy women. *Clin Imaging* 2009; 33: 462-7.
- Yoshida Y, Tsujikawa T, Kurokawa T, Tsuji T, Imamura Y, Fujibayashi Y, et al. Assessment of fluorodeoxyglucose uptake by leiomyomas in relation to histopathologic subtype and the menstrual state. *J Comput Assist Tomogr* 2009; 33: 877-81.

การสะสมน้ำตาลรังสีในเนื้ออกกล้ามเนื้อตลก: รายงานผู้ป่วย 1 ราย

สุนันทา เขียววิทย์

การนำเสนอรายโรคเนื้ออกกล้ามเนื้อตลกที่มีการสะสมน้ำตาลรังสี ผู้ป่วยหญิงอายุ 32 ปีได้รับการวินิจฉัยว่าเป็นโรคมะเร็งต่อมน้ำเหลืองชนิดฮอดกินส์ ระยะ IVb โดยมีรอยโรคที่ต่อมน้ำเหลือง supraclavicular, ต่อมน้ำเหลือง paratracheal ด้านขวา, ต่อมน้ำเหลือง subcarina, ต่อมน้ำเหลืองในช่องท้อง, ต่อมน้ำเหลือง iliac ทั้งสองข้าง, ตับ, ม้าม และไขกระดูก ผู้ป่วยได้รับการตรวจ เพท/ซีที หลังการรักษาด้วยเคมีบำบัด ผลการตรวจพบรอยโรคที่ฐานมดลูกมีลักษณะกลมที่มีสารทึบรังสีสูง และมีการสะสมน้ำตาลรังสี โดยมีปริมาณรังสี 6.3 และมีขนาด 2.0 x 1.9 เซนติเมตร ลักษณะทาง CT เข้าได้กับเนื้ออกกล้ามเนื้อตลก และไม่พบความผิดปกติอื่นจากการตรวจ เพท/ซีที ผลการตรวจ เพท/ซีที ของผู้ป่วยแสดงว่าผู้ป่วยหายจากโรค ผู้ป่วยไม่ได้ให้การรักษาเฉพาะเพียงแต่วางแผนตรวจติดตามซีที การที่ทราบการสะสมน้ำตาลรังสีในภาวะปกติ การเปลี่ยนแปลงจากภาวะปกติและผลบวกลงจากการตรวจ เพท/ซีที ทำให้มีการแปลผลการตรวจ เพท/ซีที ถูกต้องมีผลให้บอกระยะโรคถูกต้องทำให้มีการวางแผนการรักษาตรงกับระยะโรค
